UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,366	01/18/2001	Jennifer L. Hillman	PF-0293-3 DIV	1889

27904 7590 05/01/2003

INCYTE CORPORATION (formerly known as Incyte Genomics, Inc.)
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
ROARK, JESSICA H	

ART UNIT	PAPER NUMBER
1644	14

DATE MAILED: 05/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,366	HILLMAN ET AL.	
	Examiner	Art Unit	
	Jessica H. Roark	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 and 24-39* is/are pending in the application.

4a) Of the above claim(s) *24,27,29,38 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,25,26,28 and 30-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 2/19/03 (Paper No. 13), is acknowledged.
Claims 1, 11 and 22 have been cancelled. Claims 2-9, 12-21 and 23 have been cancelled previously.
Claims 10, 30 and 33 have been amended.
Claims 10 and 24-39 are pending.

Claims 24, 27, 29 and 38-39 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in Paper No. 10.

Claims 10, 25-26, 28 and 30-37 *are under consideration in the instant application.*

2. This Office Action will be in response to applicant's arguments, filed 2/19/03 (Paper No. 13). The rejections of record can be found in the previous Office Action (Paper No. 11).

It is noted that New Grounds of Rejection are set forth herein.

3. Any objection or rejection not reiterated below has been obviated by Applicant's amendment, filed 2/19/03.

Claim Objections

4. Claim 28 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form.

The definition of an "antibody" provided on page 7 of the specification does not appear to encompass labeled antibodies. Thus an antibody that is labeled is broader in scope than the antibody in the composition of claim 26.

Applicant's comments, filed 2/19/03 regarding support for labeled antibodies are acknowledged. However, at issue is whether or not the claim further limits the subject matter of the claim from which it depends. In the instant case, claim 26 does not for the reasons set forth above and of record.

35 USC § 112 first paragraph

5. Applicant's amendment, filed 2/19/03, has obviated the previous rejection of claims 10, 25-26, 28 and 30-37 under 35 U.S.C. 112, first paragraph, scope of enablement.

6. Applicant's amendment, filed 2/19/03, has obviated the previous rejection of claims 10, 25-26, 28 and 30-37 under 35 U.S.C. 112, first paragraph, written description.

35 U.S.C. §§ 102 and 103

7. Applicant is again reminded that affidavits and declarations, such as those under 37 CFR 1.131 and 37 CFR 1.132, filed during prosecution of the parent application *do not automatically become a part of this application*. Where it is desired to rely on an earlier filed affidavit, the applicant should make the remarks of record in the later application and include a copy of the original affidavit filed in the parent application.

Claim Rejections – 35 U.S.C. §§ 102 and 103

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claims 10, 26, 28 and 30-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Liu et al. (J. Biol. Chem. May 23, 1997; 272(21):13779-13785, of record, see entire document), as evidenced by the attached alignment of SEQ ID NO:1 and SWISS-PROT accession # O14734, of record.

Applicant's arguments, filed 2/19/03, have been fully considered but have not been found convincing, essentially for the reasons of record in Paper No. 11.

Applicant argues that in view of the limitation of claim 10 to recite "an isolated antibody which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:1" the rejections of record have been obviated.

The rejection of record may be found in full in Paper No. 11, and is reiterated in part below.

As previously noted residues 19-319 of the thioesterase hTE taught by Liu et al. are identical to residues 11-311 of the instant polypeptide of SEQ ID NO:1. In addition the query match between the polypeptide of SEQ ID NO:1 and hTE is 97.3%.

Liu et al. also teach the production of a polyclonal antibody to the hTE protein produced by immunizing rabbits with a fragment of hTE from Q304 to K318 (i.e., the peptide QEGVIRVKPQVSESK); the affinity purification of the antisera on hTE; and the formulation of the antisera in a composition comprising an acceptable excipient/suitable carrier (Tris neutralized glycine HCl) (see e.g., page 13780 "Co-immunoprecipitation Experiments in CEM Cells Expressing HIV-1 NefLai" and Figure 2). It is also noted that an antisera is itself is a composition comprising an antibody and an acceptable excipient.

As previously concluded, since the antisera of Liu et al. specifically binds a protein identical to instant SEQ ID NO:1 from residue 11-311, *the antisera that specifically binds hTE meets the limitations of an isolated antibody which specifically binds a polypeptide comprising the amino acid sequence of SEQ ID NO:1.*

Liu et al. further teach using the antisera to detect hTE associated with Nef in western blots (e.g., Figure 4). The Materials and Methods associated with Figure 4 (e.g., page 13780, "Co-immunoprecipitation Experiments in CEM Cells Expressing HIV-1 NefLai") further teach detection of the anti-hTE antibody using an enhanced chemiluminescence system. Thus Liu et al. also teach a composition comprising the antibody wherein the antibody is labeled, since the anti-hTE and label of the chemiluminescence system are also a composition, and the chemiluminescence system acts as a "label" for the anti-hTE antibody.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the anti-hTE antibody of Liu et al.

The reference teachings thus anticipate the instant claimed invention.

The rejection is maintained for the reasons of record.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. It is again noted that although certain broad claims are anticipated by the teachings of the references, these claims have also been included in the following rejections under 35 USC 103(a) in order to address the scope of the claims.

12. Claims 10, 26, 28 and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (J. Biol. Chem. May 23, 1997; 272(21):13779-13785, of record, in view of Zola (Monoclonal Antibodies: A Manual of Techniques, CRC Press, Boca Raton, Florida 1987, "Introduction" pages 1-11, of record).

The claims are drawn to a monoclonal antibody to a polypeptide comprising the amino acid sequence of SEQ ID NO:1, methods of making and compositions comprising said antibody.

Applicant's arguments, filed 2/19/03, have been fully considered but have not been found convincing.

Applicant argues that in view of the limitation of claim 10 to recite "an isolated antibody which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:1" the rejections of record have been obviated.

The rejection of record in full may be found in Paper No. 11.

However, as was previously noted in the rejection of record in Paper No. 11 regarding the teachings of Liu et al., and as elaborated upon supra, the antisera of Liu et al. specifically binds a protein identical to instant SEQ ID NO:1 from residue 11-311, and thus the antisera of Liu et al. meets the limitations of an isolated antibody which specifically binds a polypeptide comprising the amino acid sequence of SEQ ID NO:1.

As previously acknowledged, Liu et al. do not teach monoclonal antibodies to a polypeptide comprising an amino acid sequence of SEQ ID NO:1, methods of making and compositions comprising said antibody.

However, as previously discussed, Zola teaches production of monoclonal antibodies using techniques well known in the art at the time the invention was made (e.g., see "Title"). Zola compares in Chapter 1 monoclonal antibodies and polyclonal antibodies (antisera). Zola concludes that monoclonal antibodies are advantageous over conventional antisera when the two antibody sources are compared, and further that monoclonal antibodies can be used in situations where polyclonal antisera would not even be considered (page 9, 3rd paragraph). In particular Zola notes that monoclonal antibodies provide both an opportunity for standardization and an unlimited source of reagent versus a polyclonal antisera (page 9 "V. Monoclonal Antibodies as Standard reagents").

In particular, Zola teaches immunizing an animal with an antigen of interest, isolating antibody producing cells from the animal, fusing the antibody producing cells with immortalized cells, culturing the resulting hybridoma cells, and isolating from the culture monoclonal antibody which binds the antigen of interest (summarized in Figure 4 on page 5).

Therefore, it would have been obvious to the ordinary artisan to prepare an anti-hTE monoclonal antibody using the basic immunization strategies taught by Liu et al. (which utilizes "an immunogenic fragment of instant SEQ ID NO:1", as set forth supra), or using the full length hTE polypeptide. The ordinary artisan would have been motivated to produce a monoclonal antibody to hTE to replace the polyclonal antisera of Liu et al. because; as taught by Zola, the ordinary artisan would have expected that, among other advantages, a monoclonal antibody would provide an indefinite and easily obtainable supply of antibody (as opposed to antisera). In addition, the ordinary artisan would have been motivated to provide the monoclonal antibodies in suitable carriers such as saline or Tris buffered glycine for use in the detection methods taught by Liu et al., or for other applications involving the monoclonal antibody, since placing antibodies in pharmaceutically acceptable carriers was well known in the art at the time the invention was made. Similarly, the ordinary artisan would have been motivated to label the monoclonal antibody for use in the detection method of Liu et al. in replacement of the polyclonal antisera.

Given the teachings of Liu et al. with respect to the antigen in view of the art-recognized methodology as taught by Zola; the ordinary artisan would have had a reasonable expectation of producing a monoclonal antibody which, like the polyclonal antisera taught by Liu et al. would specifically bind the hTE polypeptide, which is identical to instant SEQ ID NO:1 from residue 11-311. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Claims 25 and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (J. Biol. Chem. May 23, 1997; 272(21):13779-13785, of record, in view of Zola (Monoclonal Antibodies: A Manual of Techniques, CRC Press, Boca Raton, Florida 1987, "Introduction" pages 1-11, of record), as applied to claims 10, 26, 28 and 33-35 above;
and further in view of Ramakrishnan et al. (US Pat. No. 5,817,310, of record).

The claims are drawn to various forms of an antibody and methods of making antibodies by screening recombinant immunoglobulin and Fab expression libraries.

Applicant's arguments, filed 2/19/03, have been fully considered but have not been found convincing.

Applicant argues that in view of the limitation of claim 10 to recite "an isolated antibody which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:1" the rejections of record have been obviated.

The rejection of record in full may be found in Paper No. 11.

However, as was previously noted in the rejection of record in Paper No. 11 regarding the teachings of Liu et al., and as elaborated upon supra, the antisera of Liu et al. specifically binds a protein identical to instant SEQ ID NO:1 from residue 11-311, and thus the antisera of Liu et al. meets the limitations of an isolated antibody which specifically binds a polypeptide comprising the amino acid sequence of SEQ ID NO:1.

Liu et al. each in view of Zola have been discussed previously and supra, and teach a monoclonal antibody to a polypeptide comprising an amino acid sequence of SEQ ID NO:1, methods of making and compositions comprising said antibody.

As previously acknowledged, Liu et al. each in view of Zola differ by not teaching chimeric, single chain, humanized or Fab/F(ab')$_2$ fragments of the antibody, nor by teaching that such antibodies can be isolated from Fab expression and recombinant immunoglobulin libraries.

However, as previously noted, one of ordinary skill in the art at the time the invention was made recognized that there were many ways to produce an antibody, and that the various forms of antibody were art-recognized variants of one another.

For example, Ramakrishnan et al. teach that the ordinary artisan at the time the invention was made recognized that antibodies could be formulated in any of a variety of interchangeable forms for use as compositions comprising a pharmaceutically acceptable carrier in a variety of art recognized assays to detect a protein of interest (see entire document, especially columns 8-17). Ramakrishnan et al. teach that antibodies can be single chain antibodies, Fab fragments, or F(ab')$_2$ fragments (see e.g. column 9 at lines 9-27), as well as chimeric antibodies (e.g., column 14). Ramakrishnan et al. also teach that it was well known in the art that antibodies to a protein of interest could produced by screening a recombinant immunoglobulin library which encode either the antibodies or fragments thereof (i.e. Fab) (e.g., see column 12 at line 56 to column 13). Further, compositions comprising antibodies in a pharmaceutically acceptable carrier, and various art recognized applications of antibodies for detection are taught in columns 15-17. Labeling of antibodies for use in various applications is also taught (e.g., column 11).

Therefore, it would have been obvious to the ordinary artisan at the time the invention was made to prepare antibodies in any of the instantly recited forms for use in art-recognized assays such as those of western blotting as taught by Liu et al.

The ordinary artisan would have been motivated to make these various forms of antibodies in view of the art-recognized interchangeability of the different antibody forms and in order to provide a variety of detection reagents that could be used in detection assays such as the western blotting assay taught by Liu et al.

The ordinary artisan recognized the advantage of antibody variants for use in such detection assays because depending upon the other antibodies used in combination, the antibody variants could be labeled using differential secondary reagents, thus avoiding high backgrounds in immunofluorescence and immunoblotting assays. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

14. No claim is allowed.

15. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
April 25, 2003

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
4/30/03